REMARKS

At the outset, it is noted that a shortened statutory response period of three (3) months was set in the April 19, 2006 Official Action. The initial due date for response, therefore, was July 19, 2006. A Petition for a One (1) Month Extension of the response period is presented with this Request for Reconsideration which is being filed before the expiration of the one (1) month extension period, as August 19, 2006 falls on a Saturday.

It is also noted, preliminarily, that a complete claim listing is not being submitted with this Request for Reconsideration. According to current PTO claim amendment practice, a complete claim listing is required only when changes are made to any claims. See http://www.uspto.gov/web/offices/pac/dapp/revised121gnas.htm.

The sole ground of rejection in the April 19, 2006 Official Action is the rejection of claims 1-3 and 5-12 under 35 USC §103(a) as allegedly unpatentable in view of the combined disclosures of Bowen et al. and Takeshima et al., both of which are references of record.

The April 19, 2006 Official Action indicates that applicants' arguments for patentability presented in response to the preceding Official Action have been considered but are not found persuasive because they are purportedly focused primarily on the difference between the claimed invention and the disclosure of Takeshima et al.

Applicants again respectfully take exception to the obviousness rejection of claims 1-3 and 5-12, which has been maintained, as well as to the Examiner's contention that applicants have not adequately addressed the rejection as based on the combined disclosures of Bowen et al. and Takeshima et al.

As pointed out in applicants' response to the preceding Official Action, the burden of establishing a *prima facie* case of obviousness falls upon the examiner. *Ex parte Wolters*, 214 USPQ 735 (Bd. Apps.1979). The record in this case clearly shows that the examiner's burden of proof has not been met. Simply stated, the combined disclosures of Bowen et al. and Takeshima et al. neither suggest to those of ordinary skill in the art that they should carry out the claimed method, nor reveal that in carrying out the claimed method, those of ordinary skill in the art would have a reasonable expectation of success. *Cf., In re Vaeck*, 20 USPQ 2d 1438 (Fed. Cir. 1991), which stands for the proposition that an obviousness rejection based on a combination of prior art references requires consideration of whether the references would have suggested to those of ordinary skill in the art that they should make the claimed

composition or device or carry out the claimed process, and whether the references would also have revealed that such person would have a reasonable expectation of success; both suggestion and expectation of success must be found in prior art, and not in applicants' disclosure.

In the July 29, 2005 Official Action, the examiner conceded, at page 22, that:

> Bowen et al. do not disclose that neuronal stem cells are co-cultured with Type 1 astrocytes of the ventral mesencephalon in order to induce the development of dopaminergic neurons.

Thus, there is no dispute that there are patentable distinctions between applicants' claimed method of inducing a dopaminergic neuronal fate in a neural stem cell or neural progenitor cell and the method for generating dopaminergic cells derived from neural precursors described in Bowen et al. In other words, it is evident that there are elements required in applicants' claims that are not present in the method described in Bowen et al.

In view of the admitted deficiencies in the disclosure of Bowen et al., it was incumbent upon the examiner, in order to meet her burden of proof under §103, to cite additional prior art that not only discloses the elements that are conceded to be missing from Bowen et al., but also provides a teaching or suggestion that would motivate one of ordinary skill in the art to modify the method of Bowen et al. to include such missing elements and thus arrive at the claimed invention. To that end, the examiner cited Takeshima et al. to provide the missing elements and the motivation that allegedly render applicants' method unpatentable. For the reasons pointed out in applicants' preceding response, however, Takeshima et al. fails to provide the elements missing from the disclosure of Bowen et al., namely, co-culturing a neural stem cell or neural progenitor cell with a Type I astrocyte of the ventral mesencephalon so as to contact the neural stem cell or neural progenitor cell with one or more astrocyte factors, and thereby induce a dopaminergic neuronal fate in the neural stem cell or neural progenitor cell. What's more, any purported motivation provided by Takeshima et al. to modify the Bowen et al. method in the manner proposed by the examiner is purely illusory.

Although the examiner has addressed applicants' arguments for patentability presented in response to the preceding Official Action, one particularly salient fact that the examiner has not refuted is that Takeshima et al. is concerned with the survival-promoting

effects of Type I astrocytes on primary cultures of the ventral mesencephalon already committed to a dopaminergic fate. Thus, there is no teaching or suggestion in Takeshima et al. of exposing immature, multipotent stem cells or progenitor cells to the dopaminergic fate-inducing effects of one or more astrocyte factors. This deficiency in the disclosure of Takeshima et al. is clearly of patentable significance, considering that the material on which a method is carried out must be accorded weight in determining the non-obviousness of the method. *Ex parte Leonard,* 187 USPQ 122 (Bd. Apps. 1974).

Turning to the motivation to modify the method of Bowen et al. purportedly provided by Takeshima et al., it is not at all evident how the combination of Bowen et al. and Takeshima et al. arguably suggests co-culturing neural stem cells or neural progenitor cells, expressing Nurr1 above basal levels, with Type I astrocytes of the ventral mesencephalon in order to induce a dopaminergic neuronal fate in the neural stem cells or neural progenitor cells, when neither reference individually provides such a suggestion. *Cf., Rockwell International Corp. v. United* States, 47 USPQ 2d 1027 (Fed. Cir. 1998). In that case, the Federal Circuit, faced with similarly deficient prior art references, reversed a holding of obviousness stating that "... with respect to obviousness, the trial court could not simply find that these four patents, when combined with each other ... taught the very limitation that admittedly none of them taught separately." Similar reasoning compels the conclusion that the §103 rejection of claims 1-3 and 5-12 cannot be maintained in this case.

The examiner plainly mischaracterizes the disclosure of Bowen et al. stating, at page 4 of the April 19, 206 Official Action, that "Bowen et al. used CNS stem cells to express Nurr 1 in a method to induce the cells to a dopaminergic phenotype and discloses that co-culturing with ventral mesencephalon astrocytes is useful for increasing survival of dopaminergic neurons." Bowen et al. nowhere suggests any benefit to be obtained by exposing neural stem or progenitor cells to ventral mesencephalon astrocyte factors. Indeed, the relevance of Bowen et al. to the present invention is limited to its disclosure that introducing the gene encoding for the nuclear receptor, Nurr1, into multipotent precursor cells from the central nervous system causes the cells to adopt a dopaminergic cell fate. The only discussion of culture conditions in Bowen et al. that the examiner refers to is in the "Background of the Invention" section, which notes that several complex mixtures or culture conditions, including co-culturing ventral mid-brain neurons with striatal astrocytes, "have been shown to increase the survival of postmitotic dopaminergic neurons." See column 3, lines 11-17 of

Bowen et al.

Takeshima et al. fails to suggest that induction of the neuronal fate can be enhanced, as exemplified in the present application, by means of astrocyte factors. Rather, Takeshima et al. describes nothing more than methods for promoting survival of dopaminergic neurons in culture.

The survival of terminally differentiated neuronal cells, and the inducement of immature-multipotent stem cells or progenitor cells to a dopaminergic phenotype are distinctly different biological processes, involving completely different cell pathways, and protocols involved in the former do not suggest themselves to those skilled in the art as having utility for improving the latter.

Regarding the lack of suggestion or motivation to combine the cited references in the manner proposed by the examiner, the present case has notable similarities to *Ex parte Levengood*, 28 USPQ 1300 (BPAI 1993). The claims under review in *Levengood* were directed to a method for increasing the proportion of mutants in a subsequent generation of a member of a plant species having a recognized and established phenotype. The method involved contacting a member of a first plant species (the recipient) with whole cells and associated materials of a second species (the donor), while the member was in a germinal stage, and simultaneously subjecting the contacted combination to electrophoretic conditions.

The claims were rejected as allegedly obvious based on the combined disclosures of three references, *Levengood* (the appellant), *Janick* and *Holl*. Like the Bowen et al. reference in this case, the *Levengood* prior art reference was concerned with the basic methodology of the claimed invention, i.e., increasing the proportion of mutants in a single plant species by applying electrical field gradients to the plant while it is in the germinal stage. However, the *Levengood* prior art reference omitted certain elements of patentable significance called for in the claimed method, as does the Bowen et al. reference in this case. Specifically, it was found that the *Levengood* prior art reference did not suggest that members of a first plant species should be placed in contact with whole cells and associated materials of a second species while simultaneously applying the electrophoretic current.

The secondary references, *Janick* and *Holl*, were not concerned with the basic methodology of the claimed invention, involving application of electrical current, but merely disclosed standard grafting and/or genetic engineering procedures. This is not unlike the Takeshima et al. in the present case, which discloses only the known survival-promoting

effect of astrocyte factors on neural cells already having the dopaminergic phenotype.

In reversing the obviousness rejection of *Levengood*, the Board stated, at 1301-1302:

> [T]he only suggestion for the examiner's combination of the isolated teachings of the applied references improperly stems from appellant's disclosure and not from the applied prior art. At best, the examiner's comments regarding obviousness amount to an assertion that one of ordinary skill in the relevant art would have been able to arrive at appellant's invention because he had the necessary skills to carry out the requisite process steps. This is an inappropriate standard for obviousness. That which is within the capabilities of one skilled in the art is not synonymous with obviousness. That one can reconstruct and/or explain the theoretical mechanism of an invention by means of logic and sound scientific reasoning does not afford the basis for an obviousness conclusion unless that logic and reasoning also supplies sufficient impetus to have led one of ordinary skill in the art to combine the teachings of the references to make the claimed invention.
>
> . . . [A]n examiner cannot establish obviousness by locating references which describe various aspects of a patent applicant's invention without also providing evidence of the motivating force which wold impel one skilled in the art to do what the patent applicant has done [Emphasis added; citations omitted].

Here, as in *Levengood*, the references cited as evidence of obviousness "fall far short of providing the 'motivation' or suggestion' to assemble their teachings into a viable process".

Furthermore, in applying the Bowen et al. and Takeshima et al. references in rejecting claims 1-3 and 5-12, the examiner appears to have ignored the well-established principle that it is improper within the framework of §103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly teaches to one of ordinary skill in the art. *In re Wesslau*, 147 USPQ 391 (CCPA 1965).

In summary, when viewed objectively and without the benefit of applicants' disclosure, the combined disclosures of Bowen et al. and Takeshima et al. fail to teach or suggest the co-culturing of neural stem cells or neural progenitor cells, expressing Nurr1 above basal levels, with Type 1 astrocytes of the ventral mesencephalon for any purpose, much less for inducing in the neural stem cells or progenitor cells a dopaminergic neuronal

fate, as recited in claims 1-3 and 5-12.

In view of the foregoing remarks, it is again respectfully requested that the rejections set forth in the April 19, 2006 Official Action be withdrawn and that this application be passed to issue, and such action is earnestly solicited.

Respectfully submitted,

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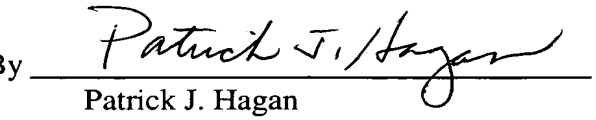
By 

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